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*       WELCOME TO THE             *
*    U.S. PATENT TEXT FILE         *
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=> s leptin

L1        38 LEPTIN

=> s ob or obesity

      4296 OB
      2564 OBESITY
L2     6710 OB OR OBESITY

=> s gene(3a)therap?

     23237 GENE
     88830 THERAP?
L3     2307 GENE(3A)THERAP?

=> s l1 or l2

L4     6725 L1 OR L2

=> s l4 and l3

L5       66 L4 AND L3

=> s l3(p)l4

L6       22 L3(P)L4

=> d 1-22
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1. 5,885,971, Mar. 23, 1999, Gene therapy by secretory gland expression; Michael German, et al., 514/44 [IMAGE AVAILABLE]

2. 5,882,860, Mar. 16, 1999, Detection of a leptin receptor variant and methods for regulating obesity; H. Ralph Snodgrass, et al., 435/6, 91.2 [IMAGE AVAILABLE]

3. 5,877,283, Mar. 2, 1999, Polypeptide for obesity and type II diabetes mellitus; Alan R. Shuldiner, et al., 530/350, 395, 827; 536/23.5 [IMAGE AVAILABLE]

4. 5,876,919, Mar. 2, 1999, Methods for identifying compounds that bind to a mammalian tub protein; Patrick W. Kleyn, et al., 435/4; 530/350 [IMAGE AVAILABLE]

5. 5,871,931, Feb. 16, 1999, Methods for detecting mammalian tub protein and RNA; Patrick W. Kleyn, et al., 435/6, 4, 7.1, 7.92, 7.95 [IMAGE AVAILABLE]

6. 5,871,697, Feb. 16, 1999, Method and apparatus for identifying, classifying, or quantifying DNA sequences in a sample without sequencing; Jonathan Marc Rothberg, et al., 422/68.1; 435/5, 6, 91.2; 536/23.1, 24.3, 24.33; 702/20 [IMAGE AVAILABLE]

7. 5,869,037, Feb. 9, 1999, Adenoviral-mediated gene transfer to adipocytes; Ronald G. Crystal, et al., 424/93.2, 93.21, 93.7; 435/320.1, 325; 514/44 [IMAGE AVAILABLE]

8. 5,861,239, Jan. 19, 1999, Methods for identifying compounds that modulate mammalian tub protein activity; Patrick W. Kleyn, et al., 435/4 [IMAGE AVAILABLE]

9. 5,856,098, Jan. 5, 1999, Detection of a leptin receptor variant; H. Ralph Snodgrass, et al., 435/6, 7.1, 7.2; 536/23.5 [IMAGE AVAILABLE]

10. 5,849,581, Dec. 15, 1998, Regulators of UCP3 gene expression; M. Catherine Amaral, et al., 435/325, 243, 320.1, 410; 536/23.1, 23.5, 24.1 [IMAGE AVAILABLE]

11. 5,849,514, Dec. 15, 1998, Method of identifying agents that modulate UCP2 promoter activity; M. Catherine Amaral, et al., 435/29, 6 [IMAGE AVAILABLE]

12. 5,837,693, Nov. 17, 1998, Intravenous hormone polypeptide delivery by salivary gland expression; Michael German, et al., 514/44; 424/93.21; 435/320.1, 325; 536/23.1 [IMAGE AVAILABLE]

13. 5,830,877, Nov. 3, 1998, Method, compositions and devices for administration of naked polynucleotides which encode antigens and immunostimulatory; Dennis A. Carson, et al., 514/44; 536/23.5, 23.51, 23.52, 24.5 [IMAGE AVAILABLE]

14. 5,817,762, Oct. 6, 1998, Mammalian tub protein; Patrick W. Kleyn, et al., 530/350; 536/23.5 [IMAGE AVAILABLE]

15. 5,807,740, Sep. 15, 1998, Regulators of UCP2 gene expression; M. Catherine Amaral, et al., 435/325, 243, 320.1, 410; 536/23.1, 24.1 [IMAGE AVAILABLE]

16. 5,766,877, Jun. 16, 1998, Genes encoding art, an agouti-related transcript; Kevin Lee Stark, et al., 435/69.1, 252.3, 254.11, 320.1, 325; 536/23.5 [IMAGE AVAILABLE]

17. 5,766,851, Jun. 16, 1998, Susceptibility gene for obesity and type II diabetes mellitus; Alan R. Shuldiner, et al., 435/6, 91.2, 810; 436/63; 536/23.5, 24.31, 24.33 [IMAGE AVAILABLE]

18. 5,723,115, Mar. 3, 1998, Inhibition of adipose tissue development and obesity; Ginette Serrero, 424/85.1, 158.1; 530/399 [IMAGE AVAILABLE]

19. 5,698,389, Dec. 16, 1997, Transcriptional promoter of the murine obesity gene; Fabienne Charles de la Brousse, et al., 435/4, 325; 536/23.1, 24.1 [IMAGE AVAILABLE]

20. 5,690,932, Nov. 25, 1997, Clinical disorders associated with carboxypeptidase E mutation; Jurgen K. Naggert, et al., 424/94.67; 435/6, 212, 219, 226; 436/63 [IMAGE AVAILABLE]

21. 5,646,040, Jul. 8, 1997, Mammalian tub gene; Patrick W. Kleyn, et al., 435/325, 320.1, 348, 357, 358, 364, 365, 369, 419; 536/23.5, 24.3, 24.31 [IMAGE AVAILABLE]

22. 5,593,837, Jan. 14, 1997, Clinical disorders associated with carboxypeptidase E mutation; J urgen K. Naggert, et al., 435/6; 424/94.63; 435/212; 436/63, 811 [IMAGE AVAILABLE]

=> d 7 kwic

US PAT NO: 5,869,037 [IMAGE AVAILABLE] L6: 7 of 22

DETDESC:

DETD(23)

Accordingly, the **therapeutic** **gene** nucleic acid sequence preferably encodes a protein selected from the group consisting of a secreted protein which acts systemically and a protein which acts upon or in the vicinity of an adipocyte. More preferably, the **therapeutic** **gene** nucleic acid sequence encodes a protein selected from the group consisting of a toxin, especially diphtheria toxin A or a. . . mouse gene (Serrero, supra), an adipsin, especially an adipsin which is a serine protease homolog (Flier et al., supra), an **Ob** protein such as a **leptin**, especially an **Ob** protein obtained from a human or mouse **obesity** gene (Zhang et al., Nature, 372, 425 (1994); Murakami et al., Biochem. Biophys. Res. Commun., 209, 944 (1995); Considine et al., J. Clin. Invest., 95, 2986 (1995)) or **OB** polypeptides such as have been described in the art (see, e.g., Great Britain Application 2,292,382), and an angiogenic substance such. . .

=> d 7 ab xa xp

US PAT NO: 5,869,037 [IMAGE AVAILABLE] L6: 7 of 22

ABSTRACT:
The present invention provides for in vivo gene transfer to adipocytes mediated by adenovirus and, in particular, the in vivo transfer of toxic genes as a means of reducing adiposity, as well as the transfer of genes encoding angiogenic substances to induce new blood vessel growth. The present invention also provides for the in vivo gene transfer to adipocytes to supply a source of proteins to be used in the local milieu of the adipocyte tissue or to be secreted and used systemically. Further, the present invention provides for the transfer of the adipocytes to other sites within a host, following adenoviral-mediated transfer of genes to the adipocytes in vivo, to allow for the exploitation of the modified adipocytes as a transferable means for the production of

protein.
ASST-EXMR: Scott D. Priebe
PRIM-EXMR: Jasemine C. Chambers

=> d l ab xa xp

US PAT NO: 5,885,971 [IMAGE AVAILABLE] L6: 1 of 22

ABSTRACT:
Secretory gland cells, particularly pancreatic and salivary gland cells, are genetically altered to operatively incorporate a gene which expresses a protein which has a desired therapeutic effect on a mammalian subject. The expressed protein is secreted directly into the gastrointestinal tract and/or blood stream to obtain therapeutic blood levels of the protein thereby treating the patient in need of the protein. The transformed secretory gland cells provide long term therapeutic cures for diseases associated with a deficiency in a particular protein or which are amenable to treatment by overexpression of a protein.
PRIM-EXMR: Bruce R. Campell

=> d clms

US PAT NO: 5,885,971 [IMAGE AVAILABLE] L6: 1 of 22

CLAIMS:

CLMS(1)

What is claimed is:

1. A method of delivering a protein to the bloodstream of a mammal, the method comprising the step of:
introducing a DNA construct into a salivary gland cell in vivo, wherein the DNA construct comprises a DNA sequence of interest which encodes a protein and a eukaryotic promoting sequence operably linked to the DNA sequence of interest;
wherein the introduced DNA construct is expressed and therotein encoded by the introduced DNA construct is delivered into the blood stream of the mammal.

CLMS(2)

2. The method of claim 1, wherein the salivary gland is a parotid gland or a submandibular gland.

CLMS(3)

3. The method of claim 1, wherein the mammal is a human and the protein is a human protein.

CLMS(4)

4. The method of claim 3, wherein the human protein is selected from the group consisting of human growth hormone and human insulin.

CLMS(5)

5. The method of claim 1, wherein said introducing is by delivery of the DNA construct into a lumen of a salivary gland duct.

CLMS(6)

6. The method of claim 1, wherein the DNA construct is not contained within a viral particle.

CLMS(7)

7. The method of claim 1, wherein said introducing is by delivery of the DNA construct into a lumen of a salivary gland duct, and the DNA construct is not contained within a viral particle.

CLMS(8)

8. The method of claim 1, wherein the protein is insulin.

CLMS(9)

9. The method of claim 1, wherein the protein is growth hormone.

CLMS(10)

10. The method of claim 1, wherein the protein is clotting factor VIII.

CLMS(11)

11. The method of claim 1, wherein the protein is erythropoietin.

=> d his

(FILE 'USPAT' ENTERED AT 15:41:53 ON 02 APR 1999)
L1 38 S LEPTIN
L2 6710 S OB OR OBESITY
L3 2307 S GENE(3A)THERAP?
L4 6725 S L1 OR L2
L5 66 S L4 AND L3
L6 22 S L3(P)L4

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